The Contribution of Higher Education and Research

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Our future is simultaneously more both exciting and threatening as never before. For example Lord Martin Rees, an astronomer, has estimated the chances of humanity surviving this century, at only 50%. There are others far more qualified than I to comment on these odds, and indeed to suggest possible interventions on climate change and global warming. But let's assume we *do* survive. As a biomedical scientist, I would like to address one of the most important issues that will then confront our children and grandchildren: ensuring that the opportunity is there for the human mind to realise its full potential.

We are undoubtedly already living longer and healthier lives. The proportion of people aged 65 and over in the UK is projected to rise from 16% in 2008 to 23% by 2033. Drug targets are set to increase from 400 to some 4,000, the genetic technologies are opening the door to much more personalised diagnosis and treatment, whilst stem cell medicine is offering a completely different strategy for treating diseases. But these indisputable advances in healthcare are themselves raising new issues relating to the mind. For example, the World Health Organisation has predicted that within this century, the biggest health problem will not be, as one might have thought, AIDS, but depression, - with an astonishing one in four of us suffering from that debilitating condition. If more of the population are reaching an age in life when the immediate preoccupations of career and child-rearing are no longer dominant, then what will we do with our lives and our time? Already an alarming number of adults are spending large amounts of money for the experience of sitting alone in front of a computer, playing games for no purpose other than the mere experience itself. Is this the apotheosis of the human condition?

Another big issue is the fact that along with an aging population, come the diseases of older people: the biggest spectre of all here, is dementia and specifically Alzheimer's Disease. There are currently approx 820,000 people with Dementia in the UK and there will be a million by 2025. The proportion of people with Dementia doubles for every five years age group with a third of people over 95 having Dementia. A shocking 1 in 3 people over 65 will die with some sort of Demetia**.** Many fear dementia more than, say, heart disease or cancer: although these are serious, often life-threatening conditions, the fact remains that you are still the person you were. With Alzheimer's disease however, the relatives and carers cannot necessarily make that claim.

If we are to focus then on challenges such as depression, well-being, and the impact of technologies on the mind, and neuro-degenerative diseases, then we need to start with the brain.

In the past, the brain and mind were regarded as distinct. The 'mind' was the province of the philosopher and thus preoccupied with exotic and insubstantial thoughts and feelings disembodied from the squalor of biology. In contrast the physical brain excited little interest in and of itself: after all it has no moving parts, has an unspectacular appearance and yields its secrets as to how it works with great reluctance. How easy, therefore, to concede to the traditional distinction of minds vs. brain of mental vs. physical. Over the last decade, however, we are starting to realise that this kind of polarisation is as unhelpful as it is unrealistic. The more we learn about the astonishing ability of the brain to adapt, "plasticity", the more we realise that the mind, one's own individual take on the world, can actually be the *personalisation* of the physical brain, through tangible, physical mechanisms.

The wonderful thing about being born a human being, as opposed to say a goldfish, is that although we are born with pretty much all the neurons we will ever have, it is the growth of connections between the brain cells that accounts for the growth of the brain after birth.

This post natal development of the human brain means that, unlike the goldfish, we have the potential for experiences to leave their mark on those brain cell connections. Let's be honest, goldfish do not have great personalities. Indeed if a goldfish died it could be interchanged with a successor purchased that day from a pet shop without the child or indeed anyone seeing the goldfish being any the wiser! But as the brain of an animal becomes more complex, so we shift from the narrow stereotype that is dictated by genes ie instinct through to learning and adaption to the environment.

We human beings don't run particularly fast, we don't see particularly well, and we are not particularly strong compared to other species in the animal kingdom: but more than any other we are fantastic at adapting; hence we occupy more ecological niches than any other species on the planet. The answer lies in a basic property of the brain, especially in the brains of humans, to adapt to every input, every moment of existence.

Let's look at one particular example of this 'plasticity'. In a particularly intriguing experiment conducted by Pascual Leone and his research group back in 1995, three groups of adult human volunteers, none of whom could play the piano, volunteered for a five day experiment. The control group, those exposed to the environment but not to the all important factor under observation, merely stared at a piano. However a second group learnt five finger piano exercises, and even over five days, showed an astonishing change in their brain scans. But, there was a third group that were more remarkable still; in this group the subjects were required merely to imagine they were playing the piano and their brain scans showed almost identical changes to those undergoing physical practice!

Once and for all then we must abandon the notion that mental doesn't have a physical basis in the brain: it does, even though how it all happens remains subject to much speculation. The old principle of "use it or lose it", just as with muscles, also applies to the brain. The more we stimulate and exercise our brain cells in different activities, the more they grow.

Growth for a brain cell is reflected in terms not of actual size of the main part of the cell but in an ever increasing and extensive growth of branches. These branches increase the surface area of a brain cell, and in turn make it a more ready target for receiving connections from other cells. Up to 100,000 brain cells will attempt to establish contact with a target cell, hence the greater the surface area the more connections can be made.

So we can see that a stimulating environment such as piano playing can actually cause brain cells to be active: in turn they will respond by growing more branches, which in turn allows them to make more cell connections. This effect can actually be seen even in rodents exposed to a so-called 'enriched' environment. 'Enriched' for rats doesn't mean that they attend interesting conferences in Hanover: rather, mere exposure to ladders and wheels and little toys will stimulate the brain sufficiently to show a growth in the extent of these branches.

It is an intriguing thought that, in the brain, this kind of change is happening for every moment we are alive. We could see therefore that even if someone is a clone, an identical twin, they will still have a unique pattern of brain cell connections; a unique mind. Imagine being born then, in the words of the great psychologist William James, into a 'booming buzzing confusion'. A baby will evaluate the world, because they can do nothing else, in terms of raw sensations: how sweet, how fast, how cold, how bright.

But gradually as a certain visual pattern accompanied possibly by certain smells and colours and textures and voices keep occurring then, as with the piano players, so certain connections will form and give each of us a personalised significance of the world. For example your mother's face, which hopefully featured regularly in your life, will have a personalised significance that it doesn't have for others' brains. It is this ability to make connections that then enables you to evaluate further inputs that I would suggest

characterises the 'growth of the mind', as we shift from a world of purely raw sensations to a more 'cognitive' world, from the Latin for 'think'. It will be a world then that has a meaning, where you have the ability to see one thing in terms of other things, such as those events and people that have already happened in your personal history.

I'm suggesting then that the mind is the personalisation of the brain, made up of unique configurations of brain cell connections, in turn driven by unique experiences in time and space, which we view as our lives, our life stories. If we adopt this neuroscientific perspective of the mind, then we can see that phrases like "blowing the mind" and "out of your mind" are surprisingly accurate. When someone puts themselves in the environment of a loud club for example with music, textures, flashing lights and repetitive beats of music, they are immersing themselves in a world much pared down in terms of cognitive content,- all in favour of a booming, buzzing confusion.

In some cases there maybe those misguided enough to take drugs which distort and thus impair further the chemical messengers at the existing connections between the brain cells. So, when we talk about a 'sensational' time perhaps we are being more literal than we could have intended: we are now re-visiting a world of raw sensations, a booming, buzzing confusion. We are 'blowing the mind' indeed 'letting ourselves go'. This notion of abrogation of the sense of self, of letting oneself go, underlies the traditional pursuits of 'wine, women and song' or 'drugs, sex and rock n'roll'. The intriguing link between, say, downhill skiing, surfing, sex, food, dancing to name but a few, is that they are all characterised by putting the notion of self on hold and of no longer being 'self-conscious', but abandoning oneself once again to raw sensations.

Sadly, however, this state of recapitulating a more childlike world, a world like that of other animals, of raw sensations, can be achieved on a more permanent basis in cases literally of loss of mind, ie dementia. We know that the pattern of growth of branches that characterises the brain from embryo to foetus, to early post natal, to mature can sadly be revisited in the opposite direction with senilities and other diseases characterised by confusion, disorientation and loss of memory, such as Alzheimer's. It is important to note here however that Alzheimer's disease is <u>not</u> a natural consequence of ageing, it is a disease of older people.

Nonetheless, one can imagine a scenario of a carefully crafted, individual brain with connections that are responding to, and activated by, and strengthened, and shaped by sequences of specific experiences that no one else has ever had, or ever will have: now imagine that those highly individualised connections are slowly dismantled as the branches shrink back. An individual would actually then become like a child again in that they would no longer have the checks and balances of the adult mind against which to evaluate ongoing experiences; people and objects would no longer have the highly personalised significance so carefully built up over a lifetime: we would see the sad and tragic symptoms of Alzheimer's disease.

To summarise so far then, I am suggesting that biological basis of the mind is the personalisation of the brain through unique dynamic configurations and neuron connections driven by unique experiences. It follows therefore that if the human brain, indeed the human mind is so sensitive to the environment, and if our environment is changing as I shall argue that it is, in a very radical way - then perhaps the human mind will be changed in a radical and unprecedented way too. This, surely, is one of the biggest challenges to our common future.

The 21st Century can be characterised, at least in the developed world, by a culture and environment increasingly dominated by Internet and video games: in some cases, addicts (with an average age of 27 years) are spending over 80 hours a week in online gaming. More recently, another study has reported that a child in the UK spends between their 10th and 11th birthdays, on average 900 hours in class, 1,277 hours with their family, and 1,934 hours in front of a screen (either television or computer). If the screen-based

lifestyle of the 21st Century is an unprecedented and pervasive phenomenon, then prolonged and frequent video gaming and Internet might surely have an unprecedented impact on the mental state of a species whose most basic talent is a highly sensitive adaptability to whatever environment in which it is placed.

Before anything, I'd like to emphasise that this impact is unlikely to be wholly good or wholly bad. Screen culture may well bring benefits such those described very eloquently by Stephen Johnson in his book, *Everything Bad is Good for You*: for example computer gaming may well be promoting higher IQ levels. An interesting reason for this might be that computer games and IQ tests are rehearsing the same kind of mental agility. However, it is mental agility that is free of context and emphasises process. We have not seen a concomitant increase in novel writing, new scientific theories,- or insights into economics, literature or history.

Mental abilities are complex and varied: so let's briefly look at some of the features that I would argue require research and attention, of relevance to both the private and public sectors of the 21st Century.

Shorter Attention span:
If the young brain is exposed from the outset to a world of fast action-reaction, of instant new screen images flashing up with each press of a key - then such rapid interchange might drive the brain into operating as default over such time scales. Perhaps when then back in the real world, such responses are not immediately forthcoming, behaviours will occur that could be regarded as Attention Deficit Hyperactivity Disorder (ADHD), and be linked to the three fold increase over that time in prescriptions for methylphenidate (Ritalin).

Living for the Moment:
The emphasis in most computer games is on the sensory-laden thrill of the moment. Perhaps not surprising then that one of the effects of video games can be an increase in physiological arousa, in turn linked to excessive release of the brain chemical dopamine. Indeed, the sheer compulsion of reliable and almost immediate reward is being linked to dopamine systems that also play a part in drug addiction. Furthermore, there is increasing evidence that excessive screen-based activities can lead to an addiction comparable to that for drugs.

Less Empathy:
In the world of the screen actions are at a premium, whilst individual thoughts would be far harder to convey with literal images. In support of the suggestion of a screen-induced decline in empathy, exposure to screen-based violence has been associated with lower empathy, whilst repeated exposure to violent video games in turn increases aggressive behaviour via changes in personality factors associated with desensitisation. Moreover, there is increasing evidence that those within the spectrum of autism (an impairment in empathy) are most comfortable in the cyber world; those within the autistic spectrum spend more time engaged with electronic screen media than any other leisure activity.

A screen by definition has to offer something arresting and literal; what you see is what you get. It is a world of action and colour and noise, how different from a book. When you play a computer game, for example to rescue the Princess, it is not because you care about the Princess but rather the thrill of the process of playing and winning the game. When you read a book, alternatively, it is because you care about the Princess. This caring empathy comes very much from reading novels and understanding how different people can see the world.

Lack of Metaphor and Abstract Concepts:
Just as it would be hard to translate feelings into literal screen images, so it would be difficult to expect current software to help the user gain a sense of abstract concepts or of metaphor. How would you show

'honour for example as a simple image, or complex lines such as 'out out brief candle , life is but a poor player…' (from Shakespeare's *Macbeth*)? Yet metaphor is a crucial hallmark of the adult human brain, that distinguishes us from even our nearest relatives, the chimps. Could constant exposure to a literal world, devoid of metaphor and abstract concepts, mean that the brain of the user remains trapped in a literal present with images that really 'mean' nothing other than what they are?

Identity:
When a human baby is born it is not self-conscious, and does not see itself as a unique and distinct being, but develops a sense of identity as he or she embarks on a unique narrative. However, if we live perpetually in the moment, in a world where events are not linked consequentially, then could our sense of self be in jeopardy? The popularity of Twitter might be an indication of need for feedback/ reassurance that one actually does exist as a unique and continuing entity. In a recent study Internet 'dependents', defined as spending more than 10 hours a week chatting/gaming, were less likely to have good coping abilities relating to their identity and intimacy. More generally, it appears that Internet addiction is accompanied by a variety of possible comorbid psychiatric disorders.

Recklessness:
Finally, another issue that may be affected by screen technologies is how reckless we are. More than any other risk taking, or rather risk management could be very important in this century: for example President Obama suggested recently that the financial crisis of the last few years, was due to greed and recklessness. After all if you play a computer game you can play the game again: actions do not have any consequences.

We know that risk taking is linked to an area in the front of the brain, the prefrontal cortex, that in biological terms is very sophisticated, occupying as it does 33% of the human brain, but only 17% of our nearest relatives, the chimps. Moreover the prefrontal cortex is a clear example of evolution being reflected in individual development: this part of the brain only becomes fully mature and active in our late teens/early twenties.

When the prefrontal cortex is damaged, patients become increasingly reckless: the first example of this was a famous case in the 1860's of a railway worker, one Phineas Gage, who had a 1.5 metre tamping iron driven through his skull by a premature explosion: he not only became reckless but also in the words of his physician was 'exceedingly capricious and childish, impatient of restraint'. Phineas had effectively recapitulated his own development.

Another group of people with an under active prefrontal cortex are those with schizophrenia, a condition not due this time to physical damage, but rather a chemical imbalance. In schizophrenia, again the world shifts from the cognitive more to a deluge of raw sensations where, like children, the patient is easily distracted, can't interpret proverbs, and takes the world literally.

A third group of those with under-active prefrontal cortex are those with a high body mass index, who are heavy in relation to their height: moreover we know that obese people, from a recent study, take more risks in gambling tasks.

What could be the common factor between gambling, eating, schizophrenia? My suggestion is that, in all of these cases, the sensory is trumping the consequences: the press of the senses, the 'here and now' environment is everything. After all, anyone who eats excessively knows the consequences, but for some the thrill of the taste trumps possible weight gain. Similarly, anyone gambling knows the consequences, but once again the thrill of the momentary experience trumps the real possibility of losing all one's money. For schizophrenics too, the sensory qualities of the outside world are distracting and over-ride the more usual 'cognitive' checks and balances that dominate in most of us.

We know that this type of common mindset, caused admittedly in different ways, is related to excessive amounts of the chemical messenger dopamine in turn leading to arousal: we've seen already dopamine also plays a part in the common underlying mechanism of most drugs of abuse. Once released we know that dopamine dampens down the prefrontal cortex. In the brain, therefore, one might imagine that engaging with computers increases arousal and in so doing releases dopamine which brings about a mindset similar to that of the child, the compulsive eater or even the schizophrenic, a world dominated by raw sensations, a "here and now" over consequences.

This list of areas for investigation are just that: possible areas for research. But I hope that you would agree that it is essential that such research is done. Just as important, at the other end of life, is to promote research into how to prevent those all-important brain cell connections can be prevented from being dismantled by diseases such as Alzheimer's.

And between the two vulnerable extremes, the very old and the very young, there is everyone else: all of us are all-important unique individuals, citizens of the 21st Century with expectations not just of living long lives, but of well-being and fulfilment. The human brain is the least understood part of our bodies and, arguably, the least understood area in biology, even in all of science. It is essential that we are able to harness all our talents and ingenuity to maximise our human potential, by investing more money in basic research. Of course, such a dream does not come cheap. But governments around the world should recognise that if research is under-funded, then the cost is far more. For example, Dementia costs the UK economy £23 billion per year. The total cost of illness of dementia disorders in EU27 in 2008 was estimated to 160 billion € of which 56% were costs of informal care. The corresponding costs for a wider EU sphere was 167 billion € and 177 billion € for the whole Europe.

"Meanwhile in the US, the public sector invests eleven-fold more in brain research than European countries, measured per capita, and the US pharmaceutical industry invests almost three times that of the European counterpart." [3]

One Australian study has shown that delaying the onset of dementia by 5 years has potential to save AUD$67.5 billion by 2040.

If we have a common future at all, then surely it will be made not just possible, but as good as possible, by doing all we can to promote the apotheosis of the human mind.
To reach this goal it is imperative that the worlds of politics, financial services, media and science converge in common debate as indeed they are this evening.

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